

Appl. No. : 09/646,950
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AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method of suppressing or inhibiting the immune response in a patient in need of such modulation, the method comprising administering to the patient an effective amount of a ~~competitive inhibitor of asparaginyl endopeptidase, wherein the competitive inhibitor is a peptide comprising an asparagine containing peptide selected from the group consisting of Ala-Glu-Asn-Lys-NH (AENK) and Lys-Asn-Asn-Glu-NH (KNNE).~~

2. (Original) A method according to Claim 1 wherein the patient has or is at risk of a disease which involves MHC Class II molecules.

3. (Currently amended) A method according to Claim 1 [[or 2]] wherein the disease is an autoimmune disease.

4. (Original) A method according to Claim 3 wherein the disease is rheumatoid arthritis.

Claims 5-11 (Cancelled)

12. (Currently amended) A method according to Claim [[11]] 62 wherein the inhibitor has the structure B1-(X)_n-Asn-Q where B1 is any suitable N terminal blocking group; X is an amino acid residue; n is between 1 and 100, Asn is an asparagine residue and Q is a group capable of reacting with the active site cysteine of asparaginyl endopeptidase.

13. (Currently amended) A method according to ~~either~~ Claim 1 [[or 2]] further comprising administering to the patient an effective amount of an agent for treatment or prevention or amelioration of an autoimmune disease or an allergic or hypersensitivity reaction.

14. (Currently amended) A method according to ~~either~~ Claim 1 [[or 2]] further comprising administering to the patient an effective amount of an immunosuppressive agent.

15. (Currently amended) A method of reducing the processing of a protein antigen by a MHC Class II molecule by a cell, the method comprising contacting the cell with an inhibitor of asparaginyl endopeptidase, wherein

the inhibitor of asparaginyl endopeptidase is a competitive inhibitor comprising a peptide selected from the group consisting of Ala-Glu-Asn-Lys-NH (AENK) and Lys-Asn-Asn-Glu-NH (KNNE); or

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the inhibitor of asparaginyl endopeptidase is a non-competitive inhibitor of asparaginyl endopeptidase which comprises an asparagine residue to which is attached a group capable of reacting with active site cysteine of asparaginyl endopeptidase.

16. (Original) A method according to Claim 15 wherein the inhibitor is a competitive inhibitor.

17. (Cancelled)

18. (Currently amended) A method according to Claim [[17]] 16 wherein the peptide is [[an]] N and C-terminal blocked peptide ~~Ala-Glu-Asn-Lys-NH (AENK) or Lys-Asn-Asn-Glu-NH (KNNE)~~.

19. (Currently amended) A method according to Claim 15 wherein the inhibitor is a non-competitive ~~or irreversible~~ inhibitor.

20. (Original) A method according to Claim 19 wherein the inhibitor has the structure B1-(X)_n-Asn-Q where B1 is any suitable N terminal blocking group; X is an amino acid residue; n is between 1 and 100, Asn is an asparagine residue and Q is a group capable of reacting with the active site cysteine of asparaginyl endopeptidase.

Claims 21-37 (Cancelled)

38. (Currently amended) A pharmaceutical composition comprising [[an]] a competitive inhibitor of asparaginyl endopeptidase and a pharmaceutically acceptable carrier,
wherein the competitive inhibitor of asparaginyl endopeptidase comprises an N and C-terminal blocked peptide selected from the group consisting of Ala-Glu-Asn-Lys-NH (AENK) and Lys-Asn-Asn-Glu-NH (KNNE).

39. (Original) A pharmaceutical composition according to Claim 38 further comprising an agent which is usefully administered to a patient in need of modulation of the immune response.

40. (Currently amended) A pharmaceutical composition according to Claim 38 further comprising [[an]] another agent for treatment or prevention or amelioration of an autoimmune disease.

41. (Original) A pharmaceutical composition according to Claim 38 further comprising an immunosuppressive agent.

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42. (Currently amended) A pharmaceutical composition comprising the composition of Claim 52 an inhibitor of asparaginyl endopeptidase, an inhibitor of cathepsin S and a pharmaceutically acceptable carrier.

Claims 43-51 (Cancelled)

52. (Original) An inhibitor of asparaginyl endopeptidase which has the structure B1-(X_aX_n)Asn-Q wherein B1 is any suitable N terminal blocking group; X_aX_n are the n amino acid residues immediately N terminal to an Asn cleavage site in the invariant chain of Class II MHC molecules; Asn is an asparagine residue; and Q is a group capable of reacting with the active site of asparaginyl endopeptidase.

53. (Previously presented) An inhibitor according to Claim 52 wherein the number of amino acid residues in (X_aX_n) is between 1 and 25.

54. (Original) An inhibitor according to Claim 53 which is any of B1-Ser-Gln-Asn-Q; B1-Leu-Glu-Asn-Q; B1-Leu-Gln-Asn-Q; B1-Pro-Glu-Asn-Q; B1-Leu-Lys-Asn-Q; B1-Gln-Asn-Q; B1-Glu-Asn-Q; B1-Asp-Glu-Asn-Q; B1-Asn-Gly-Asn-Q; B1-Phe-Pro-Asn-Q; B1-Val-Pro-Asn-Q; and B1-His-His-Asn-Q.

55. (Cancelled)

56. (Currently amended) A composition comprising an inhibitor of asparaginyl endopeptidase and an inhibitor of cathepsin S, wherein

the inhibitor of asparaginyl endopeptidase is a competitive inhibitor comprising peptide selected from the group consisting of Ala-Glu-Asn-Lys-NH (AENK) and Lys-Asn-Asn-Glu-NH (KNNE); or

the inhibitor of asparaginyl endopeptidase is a non-competitive inhibitor of asparaginyl endopeptidase which comprises an asparagine residue to which is attached a group capable of reacting with active site cysteine of asparaginyl endopeptidase.

57. (Previously presented) A method according to Claim 1 wherein the patient has or is at risk of an allergic or hypersensitivity reaction.

58. (Previously presented) A method according to Claim 1 wherein the patient has undergone or is to undergo a transplant.

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59. · (Currently amended) A method according to Claim 58 wherein the material transplanted, or to be transplanted, has been contacted with an effective amount of [[an]] the inhibitor of asparaginylendopeptidase.

60. (Previously presented) A method according to Claim 15 wherein the cell is, or is comprised in a tissue or organ, for transplantation into a patient.

61. (Previously presented) An inhibitor according to Claim 53 wherein the number of amino acid residues in (X_aX_n) is between 2 and 10.

62. (New) A method of suppressing or inhibiting the immune response in a patient in need of such modulation, the method comprising administering to the patient an effective amount of a non-competitive inhibitor of asparaginyl endopeptidase which comprises an asparagine-containing peptide and a group capable of reacting with the active site cysteine of asparaginyl endopeptidase.

63. (New) A method according to Claim 62, wherein the patient has or is at risk of a disease which involves MHC Class II molecules.

64. (New) A method according to Claim 62, wherein the disease is an autoimmune disease.

65. (New) A method according to Claim 64 wherein the disease is rheumatoid arthritis.

66. (New) A method according to Claim 62 further comprising administering to the patient an effective amount of an agent for treatment or prevention or amelioration of an autoimmune disease or an allergic or hypersensitivity reaction.

67. (New) A method according to Claim 62 further comprising administering to the patient an effective amount of an immunosuppressive agent.

68. (New) A method according to Claim 1, wherein the peptide is N and C-terminal blocked.